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March 27, 1978

Senator Edward M. Kennedy  
Chairman, Subcommittee on Health and Scientific Research  
United States Senate  
Committee on Human Resources  
Washington, D.C. 20510

Dear Senator Kennedy:

I am responding to your letter of January 31. I apologize that a number of difficulties have caused this delay. I am aware that several of my colleagues (Drs. Hoagland, Thomas and Palade) have answered your queries but we agreed to respond individually.

The questions you posed about basic research funding are penetrating and not easy to answer simply. Before answering your questions, I want to state in a general way that in the past ten years there have been two major factors which have eroded the vigor and effectiveness of American biomedical research:

1) Lack of total funds to cope with three kinds of inflations, each 10% or more annually:

- a) Cost of living and doing things
- b) Increased sophistication of biomedical technology
- c) Increased pool of highly trained researchers and desirable projects.

For lack of annual increments to meet these increased needs, the level of the research enterprise has been diminished.

2) Preference for applied research with immediate relevance and promise of quick payoffs over long-term basic studies with little promise for early solution of a disease problem.

With respect to the points raised on the first page of your letter, I have nothing to add to what Dr. Hoagland states in his letter of March 20.

Responses to the numbered questions follow:

Q. 1. Is "investigator-initiated research" an acceptable definition of "basic" research? Are not some forms of "contract" research also "basic"?

A. Contract research can have a basic research flavor and may yield results of great basic importance. However, in dealing with biologic questions, such as cancer, whose foundations are so shaky, it is generally inappropriate to make major contractual arrangements to provide these foundations. It would seem preferable to rely on the imagination and ingenuity of many individuals and small teams with modest budgets than on a few large expensive entrepreneurial efforts. In short,

it would be better to give ten \$100,000 grants than a million-dollar one, except in rare instances.

- Q.2. If we accept "investigator initiated" as synonymous with basic, what proportion of our research dollar should we invest in that category of inquiry? You suggest we return to the 1967 level of 61 percent? How do you justify choosing that particular baseline, as opposed to 30 percent, 50 percent, or 75 percent. What is so special about 1967?
- A. There is nothing special about a figure of 61% for basic research in the year 1967. However, that year marked a turning point from a confident, vigorous medical research enterprise to one which is hesitant, top heavy and dangerously unsupportive of our brightest young minds. My own assignment would be that at least 75% of the budget be allotted for basic research.
- Q.3. When you recommend 61 percent as a target, do you mean 61 percent of each institute's outlay or 61 percent of NIH's total outlays without reference to particular institutes? And if you mean the latter, how is the basic research quota to be distributed among institutes? What should the role of the Advisory Councils be under this revised system? Would they retain their role as quasi-legislative bodies which determine on a decentralized basis the appropriate distribution of dollars among research areas? What do we give up with such centralized resource allocation?
- A. Definitions and assessments of basic research funds are bound to have fuzzy edges. But the bulk of outlays can be clearly assigned to the basic research category or not. The Director of NIH should be advised in setting a clear policy and then be further advised about the annual allocation of each of the Institutes. There will be legitimate uncertainties about the basic research character of 10% of the grants but reasonable agreement about 90%.
- Q.4. Would you want us to specify in legislation that some specific proportion of research dollars should go to investigator-initiated projects?
- A. At this juncture, it would be helpful to have Congress direct a policy that would reorient biomedical research in a more basic direction.
- Q.5. What proportion should go to center grants? To education and control efforts? To intramural as opposed to extramural projects?
- A. I am unable to assign relative dollar values for center grants, educational and control programs, and intramural NIH research. Support should be extended to those of proven merit and to new proposals from gifted people. Large centers, control programs and Institutes should be compelled to weed out mediocre components.

Savings from their budgets can be used for extramural, investigator-initiated small grants.

Q.6 Is the institute structure the best way to organize research expenditures?

A. Under present circumstances, I favor continuing the current Institute structure with a view toward eventual reorganization along rational scientific and less categorical lines.

Q.7 Should all basic research dollars be spent by the Institute for General Medical Sciences? Is there such a thing as "targeted" basic research, and if not, how do we explain the often-voiced statement that the National Cancer Institute spends 50 percent of its money on "basic" research? Also, how do we reconcile the opinion of your group that NCI does "excellent" work with the fact that 64% of its money goes to "contract" work? If the work is "excellent", why change the current state of affairs?

A. I don't agree that "50% of NCI research is basic" or that "the bulk of work supported by it is excellent". Rather I believe that little of the contractual work is basic and most of it is mediocre in scientific quality. There is a vast difference between the basic orientation and overall quality of GMS research compared to NCI. Even the GMS in recent years has warped its policies and has oriented its support toward applied projects and away from basic research.

Q.8 Does the public have a role in deciding on the allocation of research dollars between categories of research expenditure? How and at what levels?

A. The public has a vital role in allocation of all public funds. They should be represented on Councils where these overall allocations are considered and reviewed. I am confident that lay representatives and members of Congress will respond to clearly presented scientific issues in a responsible and farsighted way.

Q.9 Who should do clinical trials, how should they be organized, and how much should we spend on them?

A. I do not feel confident to advise on management of clinical programs beyond insisting that their design be scientifically rigorous. I suspect that few of the current programs would meet this test.

Q.10 Should we pay for clinical procedures before they have been thoroughly tested and reviewed? Wouldn't testing them constitute

a way of preventing the indiscriminate application of half-way technologies? Or is such a plan too costly? If it were desirable, who should run it?

- A. Federal outlays for extremely costly clinical trials are usually incorrectly designated as research. This is grossly misleading. These trials are "development", in the sense of weapons testing, rather than research.

Q.11 Does multi-disciplinary research get a fair hearing at NIH currently?

- A. "Multidisciplinary" is an overworked word and issue in research. Much harm is being done by the NIH in encouraging and even coercing groups and programs to be multidisciplinary. The essence of virtually all good science today is multidisciplinary. My complaint is that the "well-rounded" programs often lack sharp cutting edges.

Q.12 Do we have enough study sections. Do we have the right kinds of study sections?

- A. I don't know whether we have enough or the right kinds of study sections. I am concerned about a number of instances in which study sections have been more interested in procedure than substance, more concerned with grantsmanship - the description of a project - than the skill and creativity of the scientist.

Q.13 Should there be a formal appeals system built into the peer-review process?

- A. I would prefer that the Director of the NIH make this judgement after appropriate study. An appeals system is likely to be costly in time and money and probably would not arrive at a better judgement after all.

Q.14 Would you recommend any changes in the internal structures, or of legal authorities for, any of the individual institutes at NIH?

- A. I am unprepared to recommend changes at this time. However, the changing face and dimensions of our scientific effort and health programs demand periodic review. As mentioned in answer to question 6, an eventual replacement of disease categories by disciplinary groupings will prove to be more economical and effective.

I apologize for the brevity of these answers.

With my warm personal regards and gratitude for your concern and action on these vital questions.

Sincerely,

Arthur Kornberg